REMARKS

Claims 29 – 39 are pending in the present application.

The Examiner has rejected claim 29-33, 35, and 37 under 35 U.S.C. § 112 first paragraph. The examiner states that the specification does reasonably provide enablement for other types of alpha-adrenoceptor antagonists and muscarinic antagonists that are not structurally related to the ones listed in claims 34 and 36. The Examiner has also rejected claims 29-38 under 35 U.S.C. § 112 first paragraph. In this rejection, the Examiner states that the subject matter was not described in the Specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor at the time the application was filed, had possession of the claimed invention. The Examiner further states that the present specification does not describe what is meant by the phrases alpha-adrenoceptor antagonists and muscarinic antagonists.

The Applicants respectfully disagree with the Examiner and request that the rejections under 35 U.S.C. § 112 first paragraph be withdrawn. The Applicants have disclosed that several types of alpha-adrenoceptor antagonists are useful for treatment of Lower Urinary Tract Symptoms (LUTS) associated with Benign Prostatic Hypertrophy (BPH) (please see Specification page 4 line 25 through page 5 line 20 and page 5 lines 10-11). The Applicants disclosure is supported by Hieble, et al. who state that several types of alpha-adrenoceptors, including alpha1 and alpha2, subtypes have shown promise in treatment of BPH (please see Hieble page 277s section 2.2.2 first paragraph, second sentence and also page 278s first paragraph second and third sentences). Thus alpha-adrenoceptor agents, generally, would be recognized by one skilled in the art to be effective in relaxing smooth muscle cells.

Additionally, the Applicants disclose that muscarinic antagonists are capable of blocking the endogenous neurotransmitter acetylcholine (please see Specification page 3 lines 23 – 27). Therefore, it is reasonable that several sub-types of the antagonist class of muscarinic active agents will have similar effects on the smooth muscle cells.

Based on the foregoing, the Applicants assert that the entirety of claimed antagonist compounds are enabled in the Application and respectfully request that the Examiner withdraw the rejection under 35 U.S.C. § 112 first paragraph on these grounds.

The Examiner has rejected claim 29-39 under 35 U.S.C. § 112 second paragraph. The examiner states that the specification is unclear as to what is meant by the phrase, "symptoms associated with benign prostatic hyperplasia". The Applicants respectfully disagree with the Examiner and request that the rejections under 35 U.S.C. § 112 second paragraph be

withdrawn. The Applicants have identified the symptoms of LUTS associated with BPH in the Specification as including "increased frequency of urination, nocturia, a poor urine stream and hesitancy or delay in starting the urine flow" (please see Specification page 1 lines 15-20).

Based on the foregoing the Applicants respectfully request that the Examiner withdraw the rejection under 35 U.S.C. § 112 second paragraph based on these grounds.

The Examiner has rejected claims 29-39 under 35 U.S.C. § 103(a) as being unpatentable over Hieble et al., in view of Ukimura. The Examiner states that Hieble teaches that one of the symptoms of BPH causes an increased resistance to the flow of urine and treatment with an alpha-adrenoceptor antagonist. The Examiner further states that Ukimura teaches administration of alpha-adrenoceptor antagonists with muscarinic receptor antagonists for the treatment of lower urinary tract conditions. The Applicants respectfully disagrees with the Examiner's characterization of the reference's teachings. The Applicants assert that there is no motivation or suggestion in the prior art to combine alpha-adrenoceptor antagonists with muscarinic receptor antagonists for the treatment of LUTS associated with BPH. In fact, Hieble et al. teach away from the use of muscarinic receptor antagonists for treatment of the symptoms associated with BPH.

Hieble et al. state that in BPH there is hyperplasia of the prostate which compresses the urethra (please see Hieble page 273s, first paragraph, first and second full sentences). Hieble identify the symptoms of BPH to be a result of increased resistance to the outflow of urine. In comparison, Hieble states that urinary incontinence affects urethral tone or inappropriate contraction of bladder detrusor muscle which can cause leakage of urine. In addition, Hieble identify neuronal which affect the bladder's ability to retain urine and obstructive conditions of the bladder which affect the bladder's ability to contract effectively (please see Hieble, page 284, section 3.1 through page 285s first full paragraph). Hieble et al., state that muscarinic receptor antagonists may be useful for treatment of conditions which involve both involuntary and voluntary contractions of the bladder, particularly for treatment of urinary incontinence, but only where lack of urinary tone is the causative factor. In conditions where outlet obstruction is the causative factor, such as BPH, muscarinic receptor antagonists it was believed by one skilled in the art, as evidenced by the teachings of Hieble et al., that further exacerbation of urinary retention would result. This effectively contra-indicates muscarinic receptor antagonists and teaches away from their use in BPH (please see Hieble page 287s section 3.2.2 first and second sentences). Hieble only identify that the use of muscarinic antagonists may be useful for conditions of increased urinary flow and do not address the use of muscarinic receptor

antagonists nor combinations of alpha-adrenoceptor antagonists with muscarinic receptor in the section of their paper which discusses the pharmacotherapy of BPH (i.e. section 2). This is because muscarinic receptor antagonists, would have been understood by one skilled in the art, at the time of Hieble, to induce increased bladder smooth muscle contractions and thus were potentially detrimental for use in conditions which are caused by increased bladder contractions or obstruction, such as BPH.

Ukimura does not mention combinations of alpha-adrenoceptor antagonists with muscarinic receptors but describes the effects of intravesicular treatment with individual agents, in relatively high local concentrations (e.g. millimolar local concentrations).

Based on the foregoing, the Applicants assert that the Examiner withdraw the rejection of claims 29 -39 under 35 U.S.C. § 103(a) on these grounds.

The Applicants believe that the application is now in condition for allowance and respectfully request early notice to that effect. If it will advance prosecution of the Application the Examiner is urged to contact the Applicants' undersigned counsel at the telephone number listed below.

Respectfully submitted,

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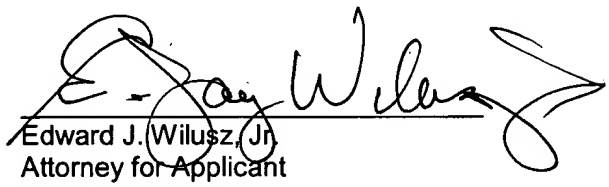

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